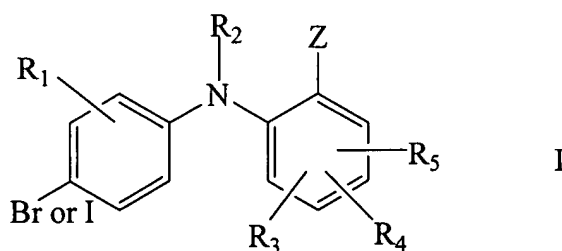


This listing of the claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-5 (cancelled).

Claim 6 (previously presented): A method for treating arthritis comprising administering to a patient suffering from arthritis and effective antiarthritic amount of a MEK inhibitor, wherein the MEK inhibitor is a compound of Formula I



wherein:

R_1 is hydrogen, hydroxy, C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo, trifluoromethyl, or CN;

R_2 is hydrogen ;

R_3 , R_4 , and R_5 independently are hydrogen, hydroxy, halo, trifluoromethyl, C_1 - C_8 alkyl, C_1 - C_8 alkoxy, nitro, CN, or $-(O \text{ or } NH)_m-(CH_2)_n-R_9$, where R_9 is hydrogen, hydroxy, COOH, or $NR_{10}R_{11}$;

n is 0-4;

m is 0 or 1;

R_{10} and R_{11} independently are hydrogen or C_1 - C_8 alkyl, or taken together with the nitrogen to which they are attached can complete a 3-10 member cyclic ring optionally containing 1, 2, or 3 additional heteroatoms selected from O, S, NH, or N- C_1 - C_8 alkyl;

Z is $COOR_7$, tetrazolyl, $CONR_6R_7$, $CONHNR_{10}R_{11}$, or CH_2OR_7 ;

R_6 and R_7 independently are hydrogen, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, (CO)- C_1 - C_8 alkyl, aryl, heteroaryl, or C_3 - C_{10} cycloalkyl optionally containing one, two,

or three heteroatoms selected from O, S, NH, or N alkyl; or R₆ and R₇ together with the nitrogen to which they are attached complete a 3-10 member cyclic ring optionally containing 1,2, or 3 additional heteroatoms selected from O, S, NH, or N alkyl; and wherein any of the foregoing alkyl, alkenyl, aryl, heterocyclic, and alkynyl groups can be unsubstituted or substituted by halo, hydroxy, C₁-C₆ alkoxy, amino, nitro, C₁-C₄ alkylamino, di(C₁-C₄) alkylamino, C₃-C₆ cycloalkyl, phenyl, phenoxy, C₃-C₅ heteroaryl, or C₃-C₅ heteroaryloxy; or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Claim 7 (currently amended): The method according to Claim 6 wherein the MEK inhibitor is a compound selected from:

[4-Chloro-2-(1H-tetrazol-5-yl)-phenyl-(4-iodo-2-methyl-phenyl)-amine;
(4-iodo-2-methyl-phenyl)-[2-(1H-tetrazol-5-yl)-phenyl]amine;
[4-nitro-2-(1H-tetrazol-5-yl)-phenyl-(4-iodo-2-methyl-phenyl)-amine;
4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid;
3,4,5-Trifluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
Sodium 5-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoate;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-2-methyl-phenylamino)-5-nitro-benzoic acid;
4-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-2-methyl-phenylamino)-benzoic acid;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
5-Iodo-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2,3,5-Trifluoro-4-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-phenylamino)-5-methoxy-benzoic acid;
5-Methyl-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-2-methyl-phenylamino)-4-nitro-benzoic acid;
2-(4-Bromo-2-methyl-phenylamino)-4-fluoro-benzoic acid;

2-(2-Bromo-4-iodo-phenylamino)-5-nitro-benzoic acid;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-benzoic acid;
5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-benzamide;
N-Ethyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N,N-dimethyl-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(1H-tetrazol-5-yl)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N,N-dimethyl-benzamide;
[5-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoylamino]-acetic acid;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-propyl-benzamide;
5-Bromo-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N,N-Diethyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N,N-Diethyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Butyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N,N-diethyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N,N-dimethyl-benzamide;
5-Bromo-3,4-difluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(2,3-Dihydroxy-propyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;
3,4-Difluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(2,3-Dihydroxy-propyl)-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
3,4-Difluoro-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyridin-4-yl-ethyl)-benzamide;

4-Fluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Bromo-N-(3-dimethylamino-propyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyridin-4-yl-ethyl)-benzamide;

N-(3-Dimethylamino-propyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-Benzyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-hydroxy-ethyl)-benzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-thiophen-2-yl-ethyl)-benzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-morpholin-4-yl-ethyl)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethylbenzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethylbenzamide;

2-(4-Bromo-2-methyl-phenylamino)-N-(3-dimethylamino-propyl)-3,4-difluorobenzenzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethylbenzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyridin-4-yl-ethyl)-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-pyridin-4-yl-ethyl)-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(3-hydroxy-propyl)-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-phenethyl-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-thiophen-2-yl-ethyl)-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-pyridin-4-ylmethyl-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-phenethyl-benzamide;

2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-piperidin-1-yl-ethyl)-benzamide;

5-Chloro-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-phenylamino)- benzamide;

5-Fluoro-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-phenylamino)- benzamide;

2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-pyridin-4-yl methyl-benzamide;

5-Bromo-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-phenylamino)- benzamide;

5-Chloro-N-(2-diethylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)- benzamide;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;

(3-Hydroxy-pyrrolidin-1-yl)-[2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-methanone;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

5-Bromo-N-(2-diethylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)- benzamide;

N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-5-chloro-2-(4-iodo-2-methyl-phenylamino)- benzamide;

N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-5-bromo-2-(4-iodo-2-methyl-phenylamino)- benzamide;

N-{3-[4-(2-Hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethyl-benzamide;

5-Bromo-2-(4-iodo-2-ethyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

5-Chloro-N-(3-dimethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-5-fluoro-2-(4-iodo-2-methyl-phenylamino)- benzamide;
5-Chloro-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-(3-diethylamino-2-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)- benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;
5-Bromo-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;
N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-2-(4-iodo-2-methyl-phenylamino)-5-nitro- benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;
5-Chloro-N-(3-diethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-(2-diisopropylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(2-piperidin-1-yl-ethyl)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperazin-1-yl-ethyl)-benzamide;
N-(2-Diethylamino-ethyl)-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-(3-dimethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(3-Hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
5-Fluoro-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(3-Diethylamino-propyl)-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(3-Diethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(3-piperidin-1-yl-propyl)-benzamide;
[5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-(3-hydroxy-pyrrolidin-1-yl)- methanone;
5-Bromo-N-(2-diisopropylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;

[5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-methanone;

N-(3-Diethylamino-2-hydroxy-propyl)-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Chloro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Fluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-Benzyloxy-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-Benzyloxy-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;

2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(4-sulfamoyl-benzyl)-benzamide;

5-Bromo-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-(2-Hydroxy-ethyl)-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-(2-Hydroxy-ethyl)-2-(4-iodo-2-ethyl-phenylamino)-5-nitro-benzamide;

2-(4-Iodo-2-methyl-phenylamino)-N-methyl-5-nitro-N-phenyl-benzamide;

5-Chloro-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;

N-Allyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-Benzyloxy-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;

N-Allyl-5-chloro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-Cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;

5-Bromo-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;

5-Iodo-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;

5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;

N-Allyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide; 2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(4-sulfamoyl-benzyl)-benzamide;

N-Allyl-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;

N-Cyclopropyl-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-Benzyloxy-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Cyclohexyl-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Allyl-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Iodo-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-5-nitro-benzamide;
5-Iodo-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-cyclohexyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;
5-Bromo-N-cyclohexyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;
N-Cyclohexyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Benzyloxy-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzyloxy-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-N-methyl-5-nitro-N-phenyl-benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-(2-Hydroxy-ethyl)-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Allyl-5-chloro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-(2-Hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
5-Fluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;
N-Cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Allyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

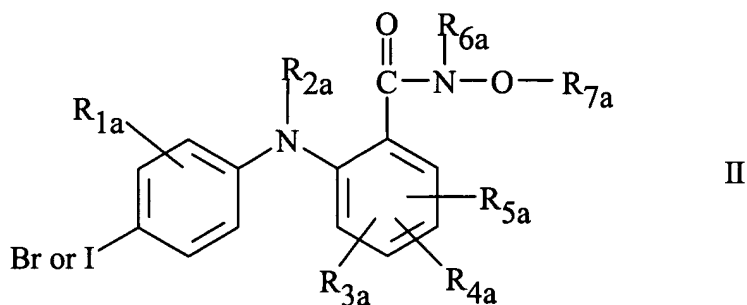
N-Benzyloxy-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Allyl-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-Allyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-benzyl alcohol;
[5-Chloro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-methanol;
[2-(4-Iodo-2-methyl-phenylamino)-5-nitro-phenyl]-methanol;
[5-Bromo-2-(4-iodo-2-methyl-phenylamino)-phenyl]-methanol; and
N-Allyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide.

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Claim 8 (previously presented): The method of claim 6, wherein the MEK inhibitor is a compound of Formula (I) wherein (a) R₁ is hydrogen, methyl, methoxy, fluoro, chloro, or bromo; (b) R₂ is hydrogen; (c) R₃, R₄, and R₅ independently are hydrogen, fluoro, chloro, bromo, iodo, methyl, methoxy, or nitro; (d) R₁₀ and R₁₁ independently are hydrogen or methyl; (e) Z is COOR₇, tetrazolyl, CONR₆R₇, CONHNR₁₀R₁₁, or CH₂OR₇; R₆ and R₇ independently are hydrogen, C₁₋₄ alkyl, heteroaryl, or C₃₋₅ cycloalkyl optionally containing one or two heteroatoms selected from O, S, or NH; or R₆ and R₇ together with the nitrogen to which they are attached complete a 5-6 member cyclic ring optionally containing 1 or 2 additional heteroatoms selected from O, NH or N-alkyl; and wherein any of the foregoing alkyl or aryl groups can be unsubstituted or substituted by halo, hydroxy, methoxy, ethoxy, or heteroaryloxy.

Claim 9 (original): The method of claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; R₃ and R₅ are independently H, fluoro, or chloro; and R₄ is fluoro.

Claim 10 (previously presented): A method for treating arthritis comprising administering to a patient suffering from arthritis and effective antiarthritic amount of a MEK inhibitor, wherein the MEK inhibitor is a compound of Formula II



wherein:

R_{1a} is hydrogen, hydroxy, C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo, trifluoromethyl, or CN;

R_{2a} is hydrogen;

R_{3a} , R_{4a} , and R_{5a} independently are hydrogen, hydroxy, halo, trifluoromethyl, C_1 - C_8 alkyl, C_1 - C_8 alkoxy, nitro, CN, or $(O \text{ or } NH)_m-(CH_2)_n-R_{9a}$, where R_{9a} is hydrogen, hydroxy, CO_2H or $NR_{10a}R_{11a}$.

n is 0-4;

m is 0 or 1;

R_{10a} and R_{11a} independently are hydrogen or C_1 - C_8 alkyl, or taken together with the nitrogen to which they are attached can complete a 3- to 10-member cyclic ring optionally containing one, two, or three additional heteroatoms selected from O, S, NH, or N- C_1 - C_8 alkyl;

R_{6a} is hydrogen, C_1 - C_8 alkyl, (CO) - C_1 - C_8 alkyl, aryl, aralkyl, or C_3 - C_{10} cycloalkyl;

R_{7a} is hydrogen, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_3 - C_{10} (cycloalkyl or cycloalkyl optionally containing a heteroatom selected from O, S, or NR_{9a});

and wherein any of the foregoing alkyl, alkenyl, aryl, heteroaryl, heterocyclic, and alkynyl groups can be unsubstituted or substituted by halo, hydroxy, C_1 - C_6 alkoxy, amino, nitro, C_1 - C_4 alkylamino, di(C_1 - C_4)alkylamino, C_3 - C_6 cycloalkyl, phenyl, phenoxy, C_3 - C_5 heteroaryl or heterocyclic radical, or C_3 - C_5 heteroaryloxy or heterocyclic radical-oxy; or R_{6a} and R_{7a} taken together with the N to which they are attached can complete a 5- to 10-membered cyclic ring, optionally

containing one, two, or three additional heteroatoms selected from O, S, or

NR_{10a}R_{11a};

or a pharmaceutically acceptable salt, ester, amide or prodrug thereof.

Claim 11 (original): The method of Claim 10, comprising a MEK inhibitor having a structure of Formula (II) wherein: (a) R_{1a} is H, methyl, fluoro, or chloro; (b) R_{2a} is H; R_{3a}, R_{4a}, and R_{5a} are each H, Cl, nitro, or F; (c) R_{6a} is H; (d) R_{7a} is methyl, ethyl, 2-propenyl, propyl, butyl, pentyl, hexyl, cyclopropylmethyl, cyclobutyl methyl, cyclopropylmethyl, or cyclopropylethyl; and (e) the 4' position is I, rather than Br.

Claim 12 (original): The method of claim 11, comprising a MEK inhibitor having a structure of Formula (II) wherein: R_{4a} is F at the 4 position, para to the CO-N-R_{6a}-OR_{7a} group and meta to the bridging nitrogen; at least one of R_{3a} and R_{5a} is F or Cl; and R_{1a} is methyl or chloro.

Claim 13 (currently amended): The method of Claim 10, comprising a MEK inhibitor having a formula selected from:

4-Fluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(methoxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(prop-2-ynyloxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-phenoxyethoxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-thienylmethoxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(prop-2-enyloxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopentoxo)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-furylmethoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-ethoxy-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(but-2-enyloxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(1-methylprop-2-ynyloxy)-
benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-phenylprop-2-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(prop-2-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(propoxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclobutyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-thienylmethoxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-methyl-prop-2-enyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-phenoxyethoxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(but-2-enyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(but-3-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopentyloxy)-benzamide;

3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-(2-fluorophenyl)-prop-2-ynyloxy)-benzamide;

5-Bromo-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(n-propoxy)-benzamide;

5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Bromo-N-(but-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide

5-Bromo-N-butoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-but-2-enyloxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-pent-2-en-4-ynyloxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-benzyl)-N-[5-(3-methoxy-phenyl)-3-methyl-pent-2-en-4-ynyloxy]-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(prop-2-ynyloxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-[3-(3-methoxy-phenyl)-prop-2-ynyloxy]-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(thiopen-2-ylmethoxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(pyridin-3-ylmethoxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-(2-fluorophenyl)-prop-2-ynyloxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(ethoxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(isopropoxy)-benzamide;

5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-but-3-ynyloxy)-benzamide;

5-Chloro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(tetrahydro-pyran-2-yloxy)-benzamide;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-methoxy-benzamide;

4-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-phenylmethoxy-benzamide;

4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-phenylmethoxy-benzamide;

5-Fluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Iodo-2-(4-iodo-2-methyl-phenylamino)-N-phenylmethoxy-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(tetrahydropyran-2-yloxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(3-phenylprop-2-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(3-furylmethoxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(2-thienylmethoxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(but-3-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(2-methyl-prop-2-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(but-2-ynyloxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(methoxy)-benzamide;

3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(ethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(cyclobutoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(isopropoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(2-phenoxyethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(n-propoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(1-methyl-prop-2-ynyloxy)-
benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(3-(3-fluorophenyl)-prop-
2-ynyloxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(4,4-dimethylpent-2-ynyloxy)-
benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(cyclopentoxy)-benzamide;
3,4,5-Trifluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
N-Hydroxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzamide;
3,4,5-Trifluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
5-Chloro-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
5-Bromo-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
2-(2-Fluoro-4-iodo-phenylamino)-N-hydroxy-4-nitro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzamide;
5-Chloro-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
5-Bromo-2-(2-bromo-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-hydroxy-4-methyl-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-5-chloro-3,4-difluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-N-hydroxy-4-nitro-benzamide;
4-Fluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
3,4-Difluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;

2-(2-Chloro-4-iodo-phenylamino)-4-fluoro-N-hydroxy-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-4-fluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-
benzamide;
5-Bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-
benzamide;
N-Cyclopropylmethoxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzamide;
N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
5-Chloro-N-cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-
benzamide;
5-Bromo-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-
benzamide;
N-Cyclopropylmethoxy-2-(2-fluoro-4-iodo-phenylamino)-4-nitro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide;
5-Chloro-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-
benzamide;
5-Bromo-2-(2-bromo-4-iodo-phenylamino)-N-ethoxy-3,4-difluoro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-ethoxy-4-nitro-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-5-chloro-N-cyclopropylmethoxy-3,4-difluoro-
benzamide
2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-nitro-benzamide;
N-Cyclopropylmethoxy-4-fluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
N-Cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-fluoro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-fluoro-benzamide; and

2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide-;
or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Claim 14 (currently amended): The method of claim 1, comprising a MEK inhibitor having a structure selected from:

2-(2-chloro-4-iodophenylamino)-5-chloro-N-cyclopropylmethoxy -3,4-difluorobenzamide;
2-(4-iodophenylamino)-N-cyclopropylmethoxy-5-chloro-3,4-difluorobenzamide;
2-(4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;
2-(2-chloro-4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;
5-chloro-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-benzoic acid; and
5-chloro-N-cyclopropylmethoxy -3,4-difluoro-2-(4-iodo-2-methylphenylamino)-benzamide ;

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Claim 15 (currently amended): A method of treating ~~or preventing~~ arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the step of administering an effective antiarthritic amount of a compound selected from:

2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-hydroxy-3,4-difluoro-5-bromobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-bromobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclobutylmethoxy-3,4-difluoro-5-bromobenzamide;
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-bromobenzamide;
2-(2-Chloro-4-iodophenylamino)-N-hydroxy-3,4-difluoro-5-bromobenzamide;
2-(2-Chloro-4-iodophenylamino)-N-cyclobutylmethoxy-3,4-difluorobenzamide;
2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;

2-(2-Methyl-4-iodophenylamino)-N-hydroxy-3,4-difluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide; and
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide- ;
or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Claim 16 (currently amended): The method of Claim 15 wherein said compound is selected from

2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide; and
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide- ;
or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

Claim 17 (currently amended): A method of treating or reducing the risk of arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the step of administering an effective antiarthritic amount of 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide-, or a pharmaceutically acceptable salt thereof.

Claim 18 (previously presented): The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; and R₃, R₄, and R₅ are independently H, fluoro, or chloro.

Claim 19 (previously presented): The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; and R₃, R₄, and R₅ independently are fluoro.

Claim 20 (previously presented): A method for treating rheumatoid arthritis comprising administering to a patient suffering from rheumatoid arthritis a therapeutically effective amount of 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide, or a pharmaceutically acceptable salt thereof.

Claim 21 (previously presented): A method for treating osteoarthritis comprising administering to a patient suffering from osteoarthritis a therapeutically effective amount of 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide, or a pharmaceutically acceptable salt thereof.

Claim 22 (new): The method for treating arthritis of Claim 6 wherein the arthritis is rheumatoid arthritis.

Claim 23 (new): The method for treating arthritis of Claim 6 wherein the arthritis is osteoarthritis.